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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,697	02/12/2001	Hagan P. Bayley	4210.001200	1449

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EXAMINER
TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/02/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/781,697	BAYLEY ET AL.	
	Examin r	Art Unit	
	My-Chau T. Tran	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-38 and 44-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-38 and 44-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed 2/13/03 in Paper No. 19 is acknowledged and entered.

Claim 32 is amended by the amendment.

2. Applicant's amendment filed 4/11/03 in Paper No. 22 is acknowledged and entered.

Claims 43-47 are added by the amendment. ***Note: Claim 43 was cancelled by the amendment filed 9/30/02 in Paper No. 17 and was one of the original filed claims that depend on the cancel Claim 42.***

Claim Objections

3. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims **43-47** (newly added claims of amendment filed 4/11/03) been renumbered **44-48**.

4. Claims 32-38 and 44-48 are pending.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 32-38 and 44-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection).

The instant claims briefly recite a method of detecting the presence of an analyte in a sample wherein the method step of contacting the sample with a pore assembly. The pore assembly comprises a modified pore subunit polypeptide covalently linked to an exogenous sensing moiety capable of preferentially binding with a specific analyte.

The specification define of "exogenous sensing moiety" is '[T]he "covalent attachment" of one or more sensing moieties to pore-forming or pore-subunit polypeptides to create the "modified, pore-forming, sensing pore-subunit polypeptides" of the present invention means that at least a first "exogenous" sensing moiety is covalently attached to the polypeptide. This differs from pore-subunit polypeptides in which the only modification(s) is one or more mutations within the amino acid sequence of the polypeptide itself. Although the sensing moiety is engineered into such polypeptides, in contrast to the native polypeptide sequence, such engineered, modified or "mutant" polypeptides still comprise an "endogenous" sensing moiety' (pg. 3, lines 10-18). The definition "exogenous sensing moiety" does not clearly distinguish it from all type of sensing moiety that specifically binds to an analyte. The specification example 3 is drawn to an oligonucleotide "exogenous sensing moiety" with a specific sequence (i.e. SEQ

ID NOs). This clearly does not provide an adequate representation regarding all type of sensing moiety that specifically binds to an analyte.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s) (e.g. all type of "exogenous sensing moiety").

In the present instance, the claimed invention contains no identifying characteristics regarding the "exogenous sensing moiety" that specifically bind to an analyte.

Additionally, the narrow scope of example 3 is directed to a specific oligonucleotide that is clearly not representative of the scope of detecting all type of analyte with any type "exogenous sensing moiety" that specifically bind to an analyte of interest of the presently claimed invention.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 32-38 and 44-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Church et al. (US Patent 5,795,782).

Church et al. discloses a method of detecting an individual polymer molecule by an interface, which comprise an ion permeable passage (col. 1, lines 35-38; col. 2, line 41-44). The ionic conductance of the passage will change as each monomer interacts. The passage is either a protein channel or a recombinant bacterial porin molecule (col. 3, line 38; col. 4, lines 57-67; fig. 2). The protein channel is assembles by covalent linkage by expressed protein (col. 3, line 38-55). The channel also includes a receptor (sensing moiety) that interacts with the polymer (col. 3, lines 28-36). The polymer to be characterized includes a portion that acts as a specific ligand for the receptor ('an exogenous sensing moiety capable of preferentially binding with a specific analyte'). The electrical current can be detected through a single channel (col. 7, lines 10-15; fig. 1 and 2) or two channels system (fig. 1 and 2). The method can also identify the individual monomers in the polymer (col. 5, lines 27-36). The polymer is any biological polymer such as DNA (col. 1, lines 59-65). The concentration of the polymer can be determined (col. 2, lines 48-58). The method of Church et al. anticipates the claimed invention.

Response to Arguments

9. Applicant's argument(s) directed to the above rejection was considered but they are not persuasive for the following reasons.

Applicant contends that "[t]here is no indication in the Church reference that any of these pore subunits are a modified pore-subunit polypeptide comprising a pore-subunit polypeptide covalently linked to an exogenous sensing moiety."

Applicant's arguments are not convincing since the Church et al. reference do teach the elements of the presently claimed invention that include the '*a modified pore-subunit polypeptide comprising a pore-subunit polypeptide covalently linked to an exogenous sensing moiety*'. Church et al. discloses several different types of protein channels or pores assemblages that can be formed from unlike molecules, e.g. a chemical pore linked to a protein polymerase (col. 3, lines 51-54) (*a pore assembly comprising one or more pore-subunit polypeptide sufficient to form a pore' and 'the pore-subunit polypeptides is a modified pore-subunit polypeptide*). The protein channels or pores assemblages comprise a sensing moiety such as a bacteriophage receptor or a nucleic acid polymerase (*exogenous sensing moiety capable of preferentially binding with a specific analyte*). Therefore, the Church et al. reference do anticipates the presently claimed invention.

10. Claims 32-33, 35 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Braha et al. (*Chemistry & Biology*, 4(7):497-505, **1997**). (Note: This rejection was incorrectly cited as a 102(e) in the previous Office Action).

Braha et al. discloses a method of detecting divalent metal ions using a bacterial pore-forming proteins, which has receptor (sensing moiety) sites and information-rich signal can be obtained by single-channel recording (pg. 498, left col., line 6 to right col., lines 1-4; pg. 502, right col., lines 8-11). The 4H subunit (pore-subunit polypeptide) was also tagged by chemical modification of a single cysteine with 4-acetamido-4'-[(iodoacetyl)amino]stibene-2-2'-disulfonate (IASD) (exogenous sensing moiety) (pg. 499, lines 51-53). In figure 1, the receptor site is shown to be a binding site for Zn^{2+} ion (pg. 498). The divalent metal ions of interest are Co(II), Ni(II), and Cu(II) (pg. 501, left col., lines 24-26). The concentration and identity of the analytes is determines by the single-channel currents to membrane potential (pg. 502, left col., lines 1-3). The method of Braha et al. anticipates the claimed invention.

Response to Arguments

11. Applicant's argument(s) directed to the above rejection was considered but they are not persuasive for the following reasons.

Applicant alleges that the Braha reference "[a]re relevant to the sensing mechanism are mutations within the amino acid sequence of the polypeptide itself, i.e. the peptides comprise only an "endogenous" sensing moiety".

Applicant's arguments are not convincing since Braha et al. do disclose an "exogenous sensing moiety". Braha et al. discloses that the 4H subunit (pore-subunit polypeptide) was also tagged by chemical modification of a single cysteine with 4-acetamido-4'-[(iodoacetyl)amino]stibene-2-2'-disulfonate (IASD) (exogenous sensing moiety) (pg. 499, lines 51-53). Therefore, Braha et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 32-38 and 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braha et al. (*Chemistry & Biology*, 4(7):497-505, **1997**) and Church et al. (US Patent 5,795,782).

Braha et al. discloses a method of detecting divalent metal ions using a bacterial pore-forming proteins, which has receptor (sensing moiety) sites and information-rich signal can be obtained by single-channel recording (pg. 498, left col., line 6 to right col., lines 1-4; pg. 502, right col., lines 8-11). In figure 1, the receptor site is shown to be a binding site for Zn^{2+} ion (pg. 498). The divalent metal ions of interest are Co(II), Ni(II), and Cu(II) (pg. 501, left col., lines 24-26). The concentration and identity of the analytes is determines by the single-channel currents to membrane potential (pg. 502, left col., lines 1-3).

The method of Braha et al. does not expressly disclose that the exogenous sensing moiety is an oligonucleotide.

Church et al. discloses a method of detecting an individual polymer molecule by an interface, which comprise an ion permeable passage (col. 1, lines 35-38; col. 2, line 41-44). The ionic conductance of the passage will change as each monomer interacts. The passage is either a protein channel or a recombinant bacterial porin molecule (col. 3, line 38; col. 4, lines 57-67; fig. 2). The protein channel is assembles by covalent linkage by expressed protein (col. 3, line 38-55). The channel also includes a receptor (sensing moiety) that interacts with the polymer (col. 3, lines 28-36). The polymer to be characterized includes a portion that acts as a specific ligand for the receptor ('an exogenous sensing moiety capable of preferentially binding with a specific analyte'). The electrical current can be detected through a single channel (col. 7, lines 10-15; fig. 1 and 2) or two channels system (fig. 1 and 2). The method can also identify the individual monomers in the polymer (col. 5, lines 27-36). The polymer is any biological polymer such as DNA (col. 1, lines 59-65). The concentration of the polymer can be determined (col. 2, lines 48-58).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the exogenous sensing moiety is an oligonucleotide as taught by Church et al. in the method of Braha et al. One of ordinary skill in the art would have been motivated to include the exogenous sensing moiety is an oligonucleotide in the method of Braha et al. for the advantage of providing a useful method for characterizing biological polymers such as deoxyribonucleic acid. Since both Braha et al. and Church et al. disclose using pore-forming

proteins for the detection of analyte (Braha: (pg. 498, left col., line 6 to right col., lines 1-4; pg. 502, right col., lines 8-11;Church: col. 1, lines 35-38; col. 2, line 41-44).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct
June 30, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER